

REMARKS

The Official Action mailed August 9, 2007, has been carefully studied, along with newly cited and applied Couser et al publication. Most of the non-elected and withdrawn claims have been cancelled without prejudice to applicants' rights to pursue such claims in one or more divisional applications, without any penalty whatsoever, if applicants choose to do so, applicants in such a case relying on Sections 121, 120 and 119.

New claim 27 has been added as a second main claim directed to the elected subject matter, and which parallels main claim 4, and is patentable for the same reasons as claim 4, as pointed out below and previously. The claims in the application are therefore now claims 4, 8, 9, 11, 14, 26 and 27. Applicants' claims define patentable subject matter and should be allowed; applicants accordingly respectfully request favorable reconsideration and allowance.

Claim 26 has been withdrawn, but no explanation has been given for such withdrawal. Claim 26 is directed to the elected subject matter, and therefore should be examined and allowed.<sup>1</sup> As pointed out on page 6 of the Reply filed March 21, 2006, claim 26 is a linking claim as it depends from and

---

<sup>1</sup> If the examiner maintains the withdrawal of claim 26, applicants **at least** deserve an explanation.

incorporates the subject matter of claim 14. Claim 11 also continues to depend from claim 14, but at least claim 11 has been examined. Claim 26, directed to the elected subject matter, should also be examined.

Claims 4, 8, 9 and 11 have been rejected under the first paragraph of Section 112 as unsupported in the original written description in the use of the word "individually" appearing in the phrase "individually isolated islets", and the word "individual" as appears in the expression "individual islet cells". The rejection is respectfully traversed.

Applicants repeat by reference the arguments previously made, which are already in the file. Moreover, attached herewith is a Declaration of an independent expert in the field, Professor James Shapiro, Director of the Clinical Islet Transplant Program at the University of Alberta in Canada, which Declaration confirms that "isolated islets" are the same as "individually isolated islets" and that this would be well understood by those skilled in the present art. Applicants respectfully remind the examiner that Professor Shapiro's Declaration is evidence which may not be properly brushed aside, and there is no evidence to the contrary.

Also see paragraphs (4)-(6) of the new (3<sup>rd</sup>) declaration of Dr. Larsson, also attached herewith.

Withdrawal of the rejection is in order and is respectfully requested.

New claim 27 has been added which is of a scope similar to that of main claim 4. The term "individually isolated islets" is not used in claim 27, and of course the term "isolated islets" is clearly supported in applicants' specification, e.g. at page 3, second paragraph.

The recitation "wherein said isolated islets are modified by irreversible adsorption of a clotting inhibiting agent comprising heparin or a fraction or derivative thereof **onto the surface of the islets**" is clearly directly supported by the description as originally filed, e.g. at page 9, last paragraph.

Claims 4, 8 and 11 have been again rejected under Section 102 as anticipated by Wagner, and applicants again respectfully traverse such rejection.

As Dr. Larsson pointed out during the interview of June 28, 2007, the examiner's interpretation of Wagner makes no sense, because, if cells of Wagner were first mixed with an anticoagulant and then encapsulated as proposed by the examiner at page 4 of the Official Action, the anticoagulant could not function because the anticoagulant would then be sealed within the microcapsule. This is confirmed as fact in

paragraph 11 of the attached Third Declaration of Professor Larsson.

In order to avoid prolixity, applicants repeat by reference the arguments previously presented against the Section 102 rejection based on Wagner.

In addition, claim 4 has been amended to recite, and new claim 27 also recites, that the islets are modified by irreversible adsorption of the heparin material "onto the surface of the islets". This is clearly not done in the prior art. There is no doubt that the encapsulation carried out by Wagner provides an insoluble polymer shell, e.g. polyamide, polyester, polyolefin, etc., around the islets, i.e. an insoluble barrier.

Contrary to this, and as stated in previously submitted Declarations, the heparin material (preferably Corline Heparin Conjugate) is adsorbed onto the cell surface with no formation of a barrier shell. Indeed, one end of the molecule is adsorbed onto the cell surface, and the other end protrudes out from the cell. Such molecules, e.g. heparin and Corline Heparin Conjugate, are water soluble molecules. The so treated islets do not delay insulin response by the cell, because there is no membrane barrier that has to be penetrated by glucose and insulin as inevitably must occur in the prior art, including Wagner.

The rejection is simply unjustified, and applicants again request that it be withdrawn.

Claims 4, 8 and 11 are again rejected under Section 102 as anticipated by Soon-Shiong. Again, this rejection is respectfully traversed, and applicants respectfully repeat by reference their earlier remarks.

Briefly, contrary to what is stated in the rejection regarding Soon-Shiong, and contrary to what Soon-Shiong discloses (see paragraphs 12 and 13 of the attached third Declaration of Professor Larsson), the clotting inhibiting agent according to applicants' claims is irreversibly adsorbed "onto the surface of the islets". Microcapsules prepared from cross-linkable polysaccharides, polycations and/or lipids per Soon-Shiong are not produced according to the present invention.

Moreover, the method of Soon-Shiong is very complicated, relying on photo-induced polymerization. It does not comply with "said modification comprising incubating said islets in a solution of heparin..." as called for in new claim 27 or by "preincubation" as called for in claim 4.

Withdrawal of the rejection is in order and is respectfully requested.

Claim 9 has been rejected as obvious under Section 103 as obvious from a combination of Soon-Shiong, Wagner and newly cited Couser. This rejection is respectfully traversed.

1. The rejection does not explain how or why Wagner and Soon-Shiong would be combined together.

2. Wagner and Soon-Shiong are both deficient for roughly the same reasons, as pointed out above, and previously. Therefore, no combination of these references could even begin to reach the subject matter of claim 4, let alone claim 9 which depends from and incorporates the subject matter of claim 4, regardless of what Couser is relied upon to show and make obvious.

3. Couser is not relevant to either Soon-Shiong or Wagner, and is certainly not relevant to the present invention. Indeed, Couser is contrary to the present invention, and such is stated as fact in paragraph 15 of the attached third Declaration of Professor Larsson.

Does the examiner dispute that Couser relates to systemic administration of a drug? If the examiner does not dispute that Couser relates to systemic administration of a drug, then applicants must ask how the Couser disclosure possibly relates to claim 9 (which incorporates claim 4) and thus relates to transplanting insulin producing cells which

Appln. No. 09/890,936  
Amd. dated December 10, 2007  
Reply to Office Action of August 9, 2007

have already been modified as recited in claim 4 together with the added subject matter of the dependent portion of claim 9.

The rejection should be withdrawn and such is respectfully requested.

The penultimate paragraph on page 9 of the Office Action states that applicant "has indicated that a copy of the Interview Summary dated June 28, 2007 has not been received." This is **not** correct. In the footnote on page 1 of applicants' "statement" filed July 30, 2007, applicants pointed out that "there is no mailing date on the Interview Summary, and applicants have still not received a **mailed** copy of the Interview Summary,...." (*emphasis added*)

Applicant's again respectfully request favorable consideration and allowance.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.  
Attorneys for Applicant

By



Sheridan Neimark  
Registration No. 20,520

SN:tdd  
Telephone No.: (202) 628-5197  
Facsimile No.: (202) 737-3528  
G:\BN\B\Bran\Korsgren1\PTO\2007-12-10AMD FRM.doc